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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/200,791	11/30/98	BEHR	T 018734/0161

HM12/1227

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EXAMINER	
BURKE, J	
ART UNIT	**PAPER NUMBER**
1642	5

DATE MAILED: 12/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/200,791	Behr et al
Examiner	**Group Art Unit**
Julie E. Burke, (Reeves), Ph.D.	1642

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-37* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-37* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Page 2 of the Oath signed by Dr. Behr is a faxed copy which is illegible. The text above the signature is not clearly legible. Therefore, the oath was not executed in accordance with either 37 CFR 1.66 or 1.68.

Also, it does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

Specification

2. The use of the trademark 'Periamin" on page 15 line 36, and in claim 19 "Onconase" for example, has been noted in this application. They should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is noted that the use of trademarks in claims is not permissible, as the meaning of the name may be changed by the owner of the trademark

during the life of the patent. Please see rejection made under 25 U.S.C. 112, second paragraph below.

3. The disclosure is objected to because of the following informalities:

The amendment to the first line of the specification does not agree with the priority statement in the Oath/Declaration. Either the first line of the specification needs to be amended or a new Oath/Declaration needs to be submitted.

Text on page 11, Section A is underlined. It is not clear if this is intended.

The Brief Description of the Drawings is incomplete as it lacks a separate description for Figures 2, 4, 6 and 7. The Brief Description of the Drawings needs to be amended so that Figures 2, 4, 6 and 7 recite separate descriptions for each view (i.e, Fig. 2A, Fig. 2B, etc.) that match the labels for the Drawings. Accordingly the brief description of the drawings should reflect this change in the numbering scheme. Also any reference to the figures should reflect the new numbering scheme.

Appropriate correction is required.

Claim Objections

4. Claim 36 is objected to because of the following informalities: text appears to be missing from the end of claim 36, as the period follows a space. It is not clear where the claim ends. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

5. Claims 2, 19, 22, 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 2 and 22 are indefinite for reciting "antibody fragment conjugates" and "metabolic products thereof" because it is not clear what fragments of products are encompassed by the scope of the claims. An antibody fragment may be as small as one amino acid in size, or even a side chain residue of a single amino acid. Similarly, the metabolic products may be small atoms. Amending the claims to recite "antigen binding fragments" and to provide a size of the metabolic product which more clearly define the structural or functional features if the conjugates and product would be sufficient to obviate this rejection.

b. Claim 19 is indefinite for reciting "or recombinant form thereof" because it is not clear how this phrase further limits the ribonuclease. A recombinant form of Onconase does not provide any limitation distinguishing the enzyme from the form as isolated from nature. Is the first recitation of onconase meant to provide a product as produced by a particular method (chemical synthesis) which would then be distinguished form the recombinantly produced onconase? Identical proteins may be produced by both recombinant and chemical methods, although glycoprotein composition and other post translational features provided by the host cell may result in a different product. As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims.

c. Claim 19 is indefinite for reciting the trademark "Onconase" because the meaning of the name may be changed to refer to other compounds during the life of the patent. Also the name is not designated as a trademark. Amending the claim to recite the common generic form of the trademark as supported by the specification as originally filed, would be sufficient to obviate this rejection.

d. Claims 24 and 25 are indefinite for reciting "the radiolabel" because it appears these claims lack proper antecedent basis for the term "radiolabel". Are the claims intended to depend upon claim 23 instead of claim 22? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims.

6. Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method recite din claim 1, wherein the protein conjugate has a molecular wight of greater than 10 kDa and less than 60 kDa, does not reasonably provide enablement for the method as recited in claim 1 or claim 18, wherein the protein conjugate has a molecular weight of less than 10 kDa or greater than 60 kDa. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a. Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount

of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

b. The claims broadly recite a method of reducing the kidney retention of a protein conjugate, wherein the protein conjugate can be of any apparent molecular weight.

c. The specification clearly states that the protein conjugates of the present invention include conjugates of molecular weight greater than about 10 kDa (page 11-12, bridging paragraph). The specification also teaches that renal retention of peptides an d small molecules is thought to occur via glomerular filtration of molecules smaller than 60 kDa (page 2, first full paragraph).

d. As evidenced by Behr et al (Eur J Nuc Med Vol 25 No 2 2/98) "the glomerulus filters proteins in a molecular weight dependent manner. If their molecular weight exceeds a molecular weight of approximately 60 kDa, these proteins are too large to be filtered through the intact glomerular basement membrane. Larger molecules, such as complete IgG with its molecular weight of 150 kDa, will therefore pass the glomerulus without appearing in the primary basement membrane" (page 202, first full paragraph). If molecules larger than 60 kDa and smaller than 1 kDa do not pass through the glomerulus, then it is not clear how they can be retained in order to practice the method as broadly claimed.

e. Additionally, the Behr Declaration field in parent application 08/407,899, states that only those proteins able to pass through an intact glomerular basement membrane will be

found in the urine, i.e., proteins that are smaller then 60 kD (paragraph 12). In view of the teachings in the specification, and in view of the admissions presented in the Behr Declaration of the parent application, one skilled in the art would not know how to reduce kidney accumulation or retention or uptake of protein conjugates with a MW >100 kD, as encompassed by the broadly written claims. Amending the claims so that they are commensurate in scope with the enablement provided by the specification as originally filed, by reciting "wherein the protein conjugate has a molecular wight of greater than 10 kDa and less than 60 kDa," would be sufficient to obviate this rejection.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,843,894. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application encompass antibody binding fragments which are recited in the

claims of the issued patent. Claims 20-22 recite the limitation of a protein conjugate which is a ribonucleic acid binding protein, including a ribonuclease or an onconase. (In view of the lacking antecedent basis claims 24-25 are being interpreted as depending upon claim 23 and not claim 22 for the instant rejection). Although the issued patent does not teach onconase, one skilled in the art would have been motivated to use the instant method for protein conjugates such as onconase because US Patent 5,595,734, filed 28 July 1992, teaches the pharmaceutical compound onconase. \

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie E. Burke, née Reeves, Ph.D, whose telephone number is (703) 308-7553. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

J Burke

Julie E. Burke, née Reeves, Ph.D.

Primary Patent Examiner

(703) 308-7553

JULIE BURKE
PRIMARY EXAMINER